

Goldstein et al.
Application No.: 10/045,903
Page 5

PATENT

Claim Listing

1. (Canceled)
2. (Currently Amended) The method of Claim 33 wherein R^3 is:
 - (a) optionally substituted heterocyclyl;
 - (b) aryl or heteroaryl both optionally substituted with a substituent selected from halo, alkyl, amino, alkoxy, carboxy, lower alkoxy carbonyl, SO_2R' (where R' is alkyl) or $SO_2NR'R''$ (where R' and R'' are independently hydrogen or alkyl);
 - (c) heteroalkyl;
 - (d) heteroalkenyl;
 - (e) heteroalkoxy;
 - (f) optionally substituted heterocyclylalkyl or heterocyclylloxy;
 - (g) optionally substituted heterocyclylalkenyl;
 - (h) optionally substituted heterocyclylalkynyl;
 - (i) optionally substituted heterocyclylalkoxy;
 - (j) optionally substituted heterocyclylalkylamino;
 - (k) optionally substituted heterocyclylalkylcarbonyl;
 - (l) $-Y-(alkylene)-R^9$ where Y is a single bond, $-O-$ or $-NH-$ and R^9 is optionally substituted heteroaryl, $-CONR^{12}R^{13}$, $-SO_2R^{14}$, $-SO_2NR^{15}R^{16}$, $-NHSO_2R^{17}$ or $-NHSO_2NR^{18}R^{19}$ where R^{12} , R^{13} , R^{14} , R^{15} , R^{16} , R^{17} , R^{18} and R^{19} are independently of each other hydrogen, alkyl or heteroalkyl;
 - (m) cycloalkylalkyl, ~~cycloalkylalkynyl~~ cycloalkylalkenyl and cycloalkylalkynyl, all optionally substituted with alkyl, halo, hydroxy or amino;
 - (n) arylaminoalkylene or heteroarylaminomalkylene; or

HALLR6 #125019 v1

Goldstein et al.
Application No.: 10/045,903
Page 6

PATENT

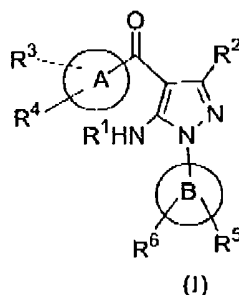
- (n) Z-alkylene-NR³⁰R³¹ where Z is -NH-, -N(alkyl)- or -O-, and R³⁰ and R³¹ are independently of each other, hydrogen, alkyl or heteroalkyl.
3. (Original) The method of Claim 2 wherein R¹ and R² are hydrogen; and B is phenyl.
4. (Original) The method of Claim 3 wherein A is phenyl.
5. (Original) The method of Claim 4 wherein R⁴ is hydrogen; and R⁵ is halo or alkyl.
6. (Original) The method of Claim 5 wherein R⁵ is chloro, fluoro or methyl; and R⁶ is hydrogen, chloro, fluoro, methyl or methoxy.
7. (Original) The method of Claim 5, wherein R³ is optionally substituted heteroaryl.
8. (Original) The method of Claim 7, wherein R³ is pyridin-2-yl, pyridin-3-yl, pyridin-4-yl, N-oxidopyridin-2-yl, N-oxidopyridin-3-yl, N-oxidopyridin-4-yl or pyridon-2-yl, all optionally substituted.
9. (Original) The method of Claim 8, wherein R³ is at the 3-position.
10. (Original) The method of Claim 9, wherein R⁵ is 4-F and R⁶ is hydrogen.
11. (Original) The method of Claim 9, wherein R⁵ is 2-Me and R⁶ is hydrogen.
12. (Original) The method of Claim 5, wherein R³ is optionally substituted phenyl.

HALLR6 #125019 v1

Goldstein et al.
Application No.: 10/045,903
Page 7

PATENT

13. (Original) The method of Claim 12, wherein R^3 is 3-sulfamoylphenyl, 3-methylsulfonylphenyl, 3-carboxyphenyl or 3-ethoxycarbonylphenyl.
14. (Original) The method of Claim 13, wherein R^3 is at the 3-position.
15. (Original) The method of Claim 14, wherein R^5 is 4-F and R^6 is hydrogen.
16. (Currently Amended) A method of treatment of a disease in a mammal treatable by administration of a p38 MAP kinase inhibitor, comprising administration to the mammal a therapeutically effective amount of a compound of Formula (I):



wherein:

R^1 is hydrogen or acyl;

R^2 is hydrogen or alkyl;

A is an aryl ring;

B is an aryl ring;

R^3 is:

[(a) heteroalkoxy;

(b) optionally substituted heterocyclalkyl;

(c) optionally substituted heterocyclalkoxy;

(d) optionally substituted heterocyclalkylamino;

(e) -Y-(alkylene)- R^9 where Y is a single bond, -O- or -NH- and R^9 is optionally substituted heteroaryl, -CONR¹²R¹³, SO₂R¹⁴, -SO₂NR¹⁵R¹⁶, -NHSO₂R¹⁷ or -NHISO₂NR¹⁸R¹⁹ where R^{12} , R^{13} , R^{14} , R^{15} , R^{16} , R^{17} , R^{18} and R^{19} are independently of each other hydrogen, alkyl or heteroalkyl;

Goldstein et al.
Application No.: 10/045,903
Page 8

PATENT

- (f) ~~heteroaryl selected from pyridinyl, N-oxidopyridinyl or pyridonyl~~
pyridin-2-yl, pyridin-3-yl, pyridin-4-yl, N-oxidopyridin-2-yl, N-
oxidopyridin-3-yl, N-oxidopyridin-4-yl or pyridon-2-yl, all optionally
substituted; or
- (g) ~~substituted-phenyl selected from sulfamoylphenyl,~~
~~methylsulfonylphenyl, carboxyphenyl or ethoxycarbonylphenyl; 3-~~
sulfamoylphenyl, 3-methylsulfonylphenyl, 3-carboxyphenyl or 3-
ethoxycarbonylphenyl;

R⁴ is:

- (a) hydrogen;
- (b) halo;
- (c) alkyl;
- (d) alkoxy; ~~||and||~~ or
- (e) hydroxy;

R⁵ is:

- (a) hydrogen;
- (b) halo;
- (c) alkyl;
- (d) haloalkyl;
- (e) thioalkyl;
- (f) hydroxy;
- (g) amino;
- (h) alkylamino;
- (i) dialkylamino;
- (j) heteroalkyl;
- (k) optionally substituted heterocycle;
- (l) optionally substituted heterocyclalkyl;
- (m) optionally substituted heterocyclalkoxy;
- (n) alkylsulfonyl;

HA11.RG #125019 v1

Goldstein et al.
Application No.: 10/045,903
Page 9

PATENT

- (o) aminosulfonyl, mono-alkylaminosulfonyl or dialkylaminosulfonyl;
- (p) heteroalkoxy; **[[and]] or**
- (q) carboxy;

R⁶ is:

- (a) hydrogen;
- (b) halo;
- (c) alkyl; **[[and]] or**
- (d) alkoxy;

or a prodrug, individual isomer, mixtures of isomers, pharmaceutically acceptable salt or solvate thereof.

17-21. (Canceled)

22. (Original) The method of Claim 16, wherein R³ is heteroalkoxy.

23. (Original) The method of Claim 22, wherein R³ is at the 3-position and is selected from the group consisting of 3-dimethylaminopropoxy, 2-dimethylaminoethoxy, 2-hydroxyethoxy, 2,3-dihydroxypropoxy, and 2,2-(dihydroxymethyl)ethoxy.

24. (Original) The method of Claim 23 wherein R⁵ is 4-F or 2-Me and R⁶ is hydrogen.

25. (Original) The method of Claim 16, wherein R³ is optionally substituted heterocyclalkyl, optionally substituted heterocyclalkoxy or optionally substituted heterocyclalkylamino.

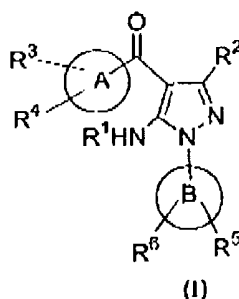
26. (Original) The method of Claim 25, wherein R³ is at the 3-position and is selected from the group consisting of 3-(morpholin-4-yl)propoxy, 2-(morpholin-4-yl)ethoxy, 2-(2-oxo-pyrrolidin-1-yl)ethoxy, 3-(morpholin-4-yl)propyl, 2-(morpholin-4-yl)ethyl, 4-(morpholin-4-yl)butyl, 3-(morpholin-4-yl)propylamino, 2-(morpholin-4-yl)ethylamino, 4-hydroxy-piperidinylmethyl, 2-(S,S-dioxo-thiamorpholin-4-yl)ethyl, 3-(S,S-dioxo-thiamorpholin-4-yl)propyl and N-methylpiperazinylmethyl.

HALLR6 #125019 v1

Goldstein et al.
Application No.: 10/045,903
Page 10

PATENT

27. (Original) The method of Claim 26 wherein R^5 is 4-F or 2-Me and R^6 is hydrogen.
28. (Original) The method of Claim 16 wherein R^3 is -Y-(alkylene)- R^9 where Y is a single bond, -O- or -NH- and R^9 is optionally substituted heteroaryl, $-\text{CONR}^{12}\text{R}^{13}$, $-\text{SO}_2\text{R}^{14}$, $-\text{SO}_2\text{NR}^{15}\text{R}^{16}$, $-\text{NHSO}_2\text{R}^{17}$ or $-\text{NHSO}_2\text{NR}^{18}\text{R}^{19}$ where R^{12} , R^{13} , R^{14} , R^{15} , R^{16} , R^{17} , R^{18} and R^{19} are independently of each other hydrogen, alkyl or heteroalkyl.
29. (Original) The method of Claim 28, wherein Y is a single bond and R^9 is $-\text{SO}_2\text{R}^{14}$ or $-\text{SO}_2\text{NR}^{15}\text{R}^{16}$.
30. (Original) The method of Claim 29 wherein R^3 is methylsulfonyl or sulfamoyl.
31. (Original) The method of Claim 30 wherein R^5 is 4-F or 2-Me and R^6 is hydrogen.
32. (Canceled)
33. (Currently Amended) A method of treatment of a disease in a mammal treatable by administration of a p38 MAP kinase inhibitor, comprising administration to the mammal a therapeutically effective amount of a compound selected from the group of compounds represented by Formula (I):



wherein:

JIA1.LR6 #125019 v1

Goldstein et al.
Application No.: 10/045,903
Page 11

PATENT

R^1 is hydrogen or acyl;

R^2 is hydrogen or alkyl;

A is an aryl ring;

B is an aryl ring;

R^3 is selected from the group consisting of:

- (a) acylamino;
- (b) optionally substituted heterocyclyl;
- (c) optionally substituted aryl or heteroaryl;
- (d) heteroalkenyl;
- (e) heteroalkynyl;
- (f) heteroalkoxy;
- (g) optionally substituted heterocyclylalkyl;
- (h) optionally substituted heterocyclylalkenyl;
- (i) optionally substituted heterocyclylalkynyl;
- (j) optionally substituted heterocyclylalkoxy, cycloxy, or heterocycloxy;
- (k) optionally substituted heterocyclylalkylamino;
- (l) optionally substituted heterocyclylalkylcarbonyl;
- (m) $-NHSO_2R^6$ where R^6 is optionally substituted heterocyclylalkyl;
- (n) $-NHSO_2NR^7R^8$ where R^7 and R^8 are, independently of each other, hydrogen, alkyl or heteroalkyl;
- (o) $-Y-(alkylene)-R^9$ where:
Y is a single bond, $-O-$, $-NH-$ or $-S(O)_n-$ (where n is an integer from 0 to 2); and R^9 is cyano, optionally substituted heteroaryl, $-COOH$, $-COR^{10}$, $-COOR^{11}$, $-CONR^{12}R^{13}$, $-SO_2R^{14}$, $-SO_2NR^{15}R^{16}$, $-NHSO_2R^{17}$ or $-NHSO_2NR^{18}R^{19}$, where R^{10} is optionally substituted heterocycle, R^{11} is alkyl, and R^{12} , R^{13} , R^{14} , R^{15} , R^{16} , R^{17} , R^{18} and R^{19} are, independently of each other, hydrogen, alkyl or heteroalkyl;

Goldstein et al.
Application No.: 10/045,903
Page 12

PATENT

- (p) $-C(=NR^{20})(NR^{21}R^{22})$ where R^{20} , R^{21} and R^{22} independently represent hydrogen, alkyl or hydroxy, or R^{20} and R^{21} together are $-(CH_2)_n-$ where n is 2 or 3 and R^{22} is hydrogen or alkyl;
- (q) $-NHC(=X)NR^{23}R^{24}$ where X is O or S, and R^{23} and R^{24} are, independently of each other, hydrogen, alkyl or heteroalkyl;
- (r) $-CONR^{25}R^{26}$ where R^{25} and R^{26} independently represent hydrogen, alkyl, heteroalkyl or optionally substituted heterocyclylalkyl, or R^{25} and R^{26} together with the nitrogen to which they are attached form an optionally substituted heterocyclyl ring;
- (s) $-S(O)_nR^{27}$ where n is an integer from 0 to 2, and R^{27} is optionally substituted heterocyclylalkyl;
- (t) cycloalkylalkyl, ~~cycloalkylalkynyl~~ cycloalkylalkenyl and cycloalkylalkynyl, all optionally substituted with alkyl, halo, hydroxy or amino;
- (u) arylaminoalkylene or heteroarylaminomethylene;
- (v) Z-alkylene- $NR^{30}R^{31}$ or Z-alkylene- OR^{32} where Z is -O-, and R^{30} , R^{31} and R^{32} are independently of each other, hydrogen, alkyl or heteroalkyl;
- (w) $-OC(O)$ -alkylene- CO_2H or $-OC(O)-NR'R''$ (where R' and R'' are independently hydrogen or alkyl); and
- (x) heteroarylalkenylene or heteroarylalkynylene;

R^4 is selected from the group consisting of:

- (a) hydrogen;
- (b) halo;
- (c) alkyl;
- (d) alkoxy; and
- (e) hydroxy;

R^5 is selected from the group consisting of:

- (a) hydrogen;

HALLR6 #125019 v1

Goldstein et al.
Application No.: 10/045,903
Page 13

PATENT

- (b) halo;
- (c) alkyl;
- (d) haloalkyl;
- (e) thioalkyl;
- (f) hydroxy;
- (g) amino;
- (h) alkylamino;
- (i) dialkylamino;
- (j) heteroalkyl;
- (k) optionally substituted heterocycle;
- (l) optionally substituted heterocyclalkyl;
- (m) optionally substituted heterocyclalkoxy;
- (n) alkylsulfonyl;
- (o) aminosulfonyl, mono-alkylaminosulfonyl or dialkylaminosulfonyl;
- (p) heteroalkoxy; and
- (q) carboxy;

R⁶ is selected from a group consisting of:

- (a) hydrogen;
- (b) halo;
- (c) alkyl; and
- (d) alkoxy; and

prodrugs, individual isomers, mixtures of isomers and pharmaceutically acceptable salts thereof.

34-37. (Canceled)

38. (Previously Presented). The method of Claim 33 wherein the disease is rheumatoid arthritis.

HALIR6 #125019 v1

Goldstein et al.
Application No.: 10/045,903
Page 14

PATENT

39. (Previously Presented). The method of Claim 33 wherein the disease is adult respiratory distress syndrome.
40. (Previously Presented). The method of Claim 33 wherein the disease is asthma.
41. (Canceled)
42. (Currently Amended) The method of claim 16, wherein R^3 is optionally substituted ~~heteroaryl selected from~~ pyridinyl, N-oxidopyridinyl or pyridonyl.
43. (Currently Amended) The method of claim 42, wherein R^3 is pyridin-2-yl, pyridin-3-yl, pyridin-4-yl, N-oxidopyridin-2-yl, N-oxidopyridin-3-yl, N-oxidopyridin-4-yl or pyridon-2-yl, each of which may be optionally substituted.
44. (Canceled)
45. (Currently Amended) The ~~compound~~method of claim 28, wherein R^3 is -(alkylene)- $SO_2NR^{34}R^{35}$ where R^{34} and R^{35} each independently is hydrogen or alkyl.

HALLR6 #125019 v1